

**TRADE SECRET**

*Study Title*

**H-28548: COMBINED CHRONIC TOXICITY/ONCOGENICITY  
STUDY 2-YEAR ORAL GAVAGE STUDY IN RATS**

Laboratory Project ID: DuPont-18405-1238

**Volume 8 of 13**

**NUMBER OF PAGES IN VOLUME:** 351

- TEST GUIDELINES:**
- U.S. EPA Health Effects Test Guidelines OPPTS 870.4300 Combined Chronic Toxicity/Carcinogenicity (1998)
  - OECD Guidelines for the Testing of Chemicals Section 4 (No. 453) Health Effects (2009)
  - JMAFF Japan Agricultural Chemicals Regulation Law 12 Nousan No. 8147 (2000)
  - EEC Methods for the Determination of Toxicity Method B.33 Combined Chronic/Carcinogenicity test, Directive 88/302/EC (1988)

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**STUDY COMPLETED ON:** March 28, 2013

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**MPI RESEARCH STUDY NUMBER:** 125-141

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MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1109	S	<b>Microscopic</b> pancreas  testes tongue	- carcinoma, islet cell, malignant, primary, incidental, not cause of death - hyperplasia, acinar cell, focal, mild - within normal limits - within normal limits
1110	E	<b>Macroscopic</b> kidneys lymph node, inguinal  lymph node, mesenteric  pancreas  skin, subcutis	- cyst, clear, left, mild - within normal limits draining node for mass a, left. - within normal limits draining node for mass b and mass c. - mass, tan, mass b, present approximately 0.9 cm in diameter. - mass, tan, mass a, inguinal, left, present corresponds to antemortem observation (swelling hair sparse mass 1 scabbed area) approximately 3.0 x 2.5 x 1.0 cm.

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1110	E	<b>Macroscopic</b> small intestine, jejunum	- mass, tan, mass c, present approximately 0.6 cm in diameter.
1110	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt	- pheochromocytoma, benign, bilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1110	E	<b>Microscopic</b> harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric	- within normal limits - cardiomyopathy, minimal - within normal limits - cyst, unilateral, moderate corresponds to macroscopic observation (kidneys - cyst) - hydronephrosis, unilateral, mild - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - infiltration, mononuclear cell, minimal - vacuolation, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1110	E	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands  pharynx pituitary gland  preputial glands  prostate gland salivary gland, mandibular salivary gland, parotid	- degeneration, axonal/myelin, moderate - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, islet cell, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (pancreas - mass b) - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - carcinoma, squamous cell, malignant, unilateral, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - inflammation, acute, moderate - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1110	E	<b>Microscopic</b> salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris  skin  small intestine, duodenum small intestine, ileum small intestine, jejunum  spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes	- within normal limits - within normal limits - atrophy, mild - degeneration/necrosis, myofiber, mild - erosion/ulcer, moderate corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - adenocarcinoma, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (small intestine, jejunum - mass c) - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1110	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - gastrointestinal tumor
1111	E	<b>Macroscopic</b> esophagus eyes  pituitary gland	- foreign material, moderate - discoloration, red, left, moderate corresponds to antemortem observation (eye discolored) - enlarged, mild
1111	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1111	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes  eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hemorrhage, unilateral, mild corresponds to macroscopic observation (eyes - discoloration, red) - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1111	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid	- within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1111	E	<b>Microscopic</b> salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1111	E	<b>Microscopic</b> urinary bladder non-correlated macro observation Cause of Death	- within normal limits - pituitary gland - enlarged - undetermined
1112	S	<b>Macroscopic</b> skin	- nodule, black, dorsal cervical region, present corresponds to antemortem observation (nodule) approximately 1.0 cm in diameter.
1112	S	<b>Microscopic</b> liver  pancreas	- degeneration, cystic, focal, mild - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - vacuolation, midzonal, mild - adenoma, islet cell, benign, primary, incidental, not cause of death
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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1112	S	<b>Microscopic</b> skin	- carcinoma, squamous cell, malignant, primary, mortality-independent corresponds to macroscopic observation (skin - nodule)
		testes	- within normal limits
		tongue	- within normal limits
1113	E	<b>Macroscopic</b> kidneys	- irregular surface, tan, bilateral, mild
		lymph node, inguinal	- not identified, left, no grade draining node for mass a.
		skin, subcutis	- mass, tan, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 13.0 x 7.6 x 7.4 cm.
1113	E	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, minimal - pheochromocytoma, benign, unilateral, primary, incidental, not cause of death

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1113	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- within normal limits - hyperplasia, granulocytic, mild - hyperplasia, granulocytic, mild - within normal limits - within normal limits - within normal limits - depletion, secretory, bilateral, moderate - oligospermia/germ cell debris, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface) - thrombus, unilateral, mild

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1113	E	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, eosinophilic, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits - cyst, mild

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1113	E	<b>Microscopic</b> prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	 - within normal limits - within normal limits - within normal limits - within normal limits - depletion, secretory, bilateral, moderate - within normal limits - within normal limits - fibrosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1113	E	<b>Microscopic</b> testes	- adenoma, interstitial cell, benign, unilateral, primary, incidental, not cause of death
		thymus	- degeneration/atrophy, seminiferous tubules, bilateral, mild
		thyroid gland	- depletion, lymphoid, generalized, moderate
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- one of pair present
		Cause of Death	- within normal limits
1114	E	<b>Macroscopic</b> foot/feet	- fibrosarcoma/fibroma
			- swollen/thickened, bilateral, mild
			corresponds to antemortem observation (swelling)
1114	E	<b>Microscopic</b> adrenal glands	- within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1114	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina foot/feet  galt harderian glands heart joint, tibiofemoral	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - osteoarthritis/pododermatitis, bilateral, severe corresponds to macroscopic observation (foot/feet - swollen/thickened) - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1114	E	<b>Microscopic</b> kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	- nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - vacuolation, periportal, minimal - macrophages, pigmented alveolar, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1114	E	<b>Microscopic</b> pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus	   - hyperplasia, focal, pars distalis, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1114	E	<b>Microscopic</b> thyroid gland tongue trachea ureters  urinary bladder Cause of Death	- cyst, follicular, unilateral, mild - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - osteoarthritis/pododermatitis
1115	E	<b>Macroscopic</b> kidneys lymph node, inguinal  lymph node, mandibular  mesentery/peritoneum	- cyst, red, left, mild - within normal limits draining node for mass b, bilateral. - within normal limits draining node for mass a, bilateral. - nodule, tan, multiple, present approximately 0.45 cm in diameter.
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1115	E	<b>Macroscopic</b> skin	- abrasion/scab, left lateral abdomen, moderate corresponds to antemortem observation (scabbed area) - mass, tan, mass b, dorsal lumbar region, present corresponds to antemortem observation (nodule) approximately 3.0 x 2.5 x 1.0 cm. - mass, tan, mass a, ventral neck, present corresponds to antemortem observation (mass 1) approximately 9.0 cm in diameter.
1115	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides	- vacuolation, focal, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1115	E	<b>Microscopic</b> esophagus eyes eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - schwannoma, malignant, primary, incidental, not cause of death - within normal limits - cyst, unilateral, mild corresponds to macroscopic observation (kidneys - cyst) - nephropathy, chronic progressive, bilateral, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal
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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1115	E	<b>Microscopic</b> lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland	- hyperplasia, type II cell, mild - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, islet cell, malignant, multiple, primary, incidental, not cause of death corresponds to macroscopic observation (mesentery/peritoneum - nodule) - hyperplasia, acinar cell, focal, minimal - not examined - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - cyst, mild

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1115	E	<b>Microscopic</b> prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- within normal limits</li> <li>- adenoma, sebaceous cell, benign, primary, incidental, not cause of death small tumor on slide 18-2.</li> <li>- crust, serocellular, moderate corresponds to macroscopic observation (skin - abrasion/scab)</li> <li>- erosion/ulcer, mild corresponds to macroscopic observation (skin - abrasion/scab)</li> <li>- hyperplasia, epidermal, moderate corresponds to macroscopic observation (skin - abrasion/scab)</li> <li>- papilloma, squamous cell, benign, primary, mortality-independent corresponds to macroscopic observation (skin - mass b)</li> <li>- lipoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)</li> </ul>
		skin, subcutis	<ul style="list-style-type: none"> <li>- lipoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)</li> </ul>
		small intestine, duodenum	<ul style="list-style-type: none"> <li>- within normal limits</li> </ul>

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1115	E	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - polyarteritis, bilateral, mild - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - lipoma/liposarcoma
1116	D	<b>Macroscopic</b> eyes	- absent/cannibalized, bilateral, no grade

E - Euthanized *in extremis*  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1116	D	<b>Macroscopic</b> eyes, optic nerves eyes, retina harderian glands lacrimal glands, exorbital larynx lymph node, mandibular pharynx salivary gland, mandibular salivary gland, parotid salivary gland, sublingual spinal cord, cervical thyroid/parathyroid glands tongue trachea	- absent/cannibalized, bilateral, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, left, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, no grade - absent/cannibalized, no grade
1116	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1116	D	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes  eyes, optic nerves  eyes, retina  galt harderian glands  heart joint, tibiofemoral kidneys	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined cannibalized - not examined cannibalized - not examined cannibalized - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1116	D	<b>Microscopic</b> lacrimal glands, exorbital	- not examined cannibalized
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- not examined cannibalized
		liver	- vacuolation, centrilobular, minimal
		lung	- bacterial colonies, mild - macrophages, alveolar, mild
		lymph node, mandibular	- not examined cannibalized
		lymph node, mesenteric	- within normal limits
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		pancreas	- within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1116	D	<b>Microscopic</b> parathyroid glands	- not examined cannibalized
		pharynx	- not examined cannibalized
		pituitary gland	- within normal limits
		prostate gland	- within normal limits
		salivary gland, mandibular	- not examined cannibalized
		salivary gland, parotid	- not examined cannibalized
		salivary gland, sublingual	- not examined cannibalized
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1116	D	<b>Microscopic</b> spinal cord, cervical  spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue  trachea  ureters urinary bladder Cause of Death	- within normal limits spinal cord is present. - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined cannibalized - not examined cannibalized - within normal limits trachea is present. - within normal limits - within normal limits - dosing injury
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1117	E	<b>Macroscopic</b> eyes  hind limb/leg	- discoloration, white, bilateral, mild corresponds to antemortem observation (eye discolored) - discoloration, red, left, moderate corresponds to antemortem observation (skin discolored swelling)
1117	E	testes <b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes  eyes, optic nerves	- small, right, mild  - vacuolation, focal, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - oligospermia/germ cell debris, unilateral, severe - within normal limits - cataract, bilateral, moderate corresponds to macroscopic observation (eyes - discoloration, white) - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1117	E	<b>Microscopic</b> eyes, retina galt harderian glands heart hind limb/leg  joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular	- fold/rosette, retinal, unilateral, mild - within normal limits - within normal limits - cardiomyopathy, mild - inflammation, moderate corresponds to macroscopic observation (hind limb/leg - discoloration, red) - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1117	E	<b>Microscopic</b> lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - hyperplasia, focal, pars distalis, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1117	E	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes  thymus thyroid gland tongue trachea ureters urinary bladder	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration/atrophy, seminiferous tubules, unilateral, severe corresponds to macroscopic observation (testes - small) - hemangioma, benign, unilateral, primary, incidental, not cause of death - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1117	E	<b>Microscopic</b> Cause of Death	- hind limb/leg; inflammation; moderate
1118	E	<b>Macroscopic</b> lacrimal glands, exorbital liver lymph node, mandibular pituitary gland stomach, glandular stomach, nonglandular testes	- small, bilateral, mild - discoloration, tan, multiple lobes, moderate - enlarged, bilateral, mild - enlarged, red, severe - focus/foci, brown, mild - swollen/thickened, limiting ridge, mild - enlarged, bilateral, moderate
1118	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur	- hyperplasia, focal medullary, bilateral, mild - pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - vacuolation, focal, unilateral, minimal - mineralization, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1118	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital  large intestine, cecum	- within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - depletion, secretory, bilateral, severe - oligospermia/germ cell debris, bilateral, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, severe - depletion, secretory, bilateral, moderate corresponds to macroscopic observation (lacrimal glands, exorbital - small) - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1118	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular  lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b	- within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, mild - vacuolation, periportal, severe corresponds to macroscopic observation (liver - discoloration, tan) - histiocytosis, alveolar, minimal - dilatation, sinus, mild corresponds to macroscopic observation (lymph node, mandibular - enlarged) - hyperplasia, lymphocyte/plasmacyte, medulla, mild corresponds to macroscopic observation (lymph node, mandibular - enlarged) - within normal limits - dilatation, gland/lumen, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1118	E	<b>Microscopic</b> nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits - within normal limits - hyperplasia, acinar cell, focal, moderate - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - depletion, secretory, bilateral, severe - within normal limits - within normal limits - hyperplasia, mucosal, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1118	E	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - erosion/ulcer, mild corresponds to macroscopic observation (stomach, glandular - focus/foci, brown) - hyperplasia, mucosal, mild corresponds to macroscopic observation (stomach, glandular - focus/foci, brown)
		stomach, nonglandular	- hyperplasia, epithelial, limiting ridge, mild corresponds to macroscopic observation (stomach, nonglandular - swollen/thickened)
		testes	- degeneration/atrophy, seminiferous tubules, bilateral, severe - edema, bilateral, moderate corresponds to macroscopic observation (testes - enlarged)
		thymus	- depletion, lymphoid, generalized, mild - hyperplasia, lymphoid, medulla, minimal
		thyroid gland	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1118	E	<b>Microscopic</b> tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1119	D	<b>Macroscopic</b> all tissues	- within normal limits
1119	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*  
D - Died on Study



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1119	D	<b>Microscopic</b> epididymides esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular	- within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - bacterial colonies, mild - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1119	D	<b>Microscopic</b> lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1119	D	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1120	S	<b>Macroscopic</b> adrenal glands	- enlarged, left, mild
1120	S	<b>Microscopic</b> adrenal glands	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (adrenal glands - enlarged)

S - Scheduled necropsy  
D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1120	S	<b>Microscopic</b> liver	- focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal
		pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death - atrophy, acinar, mild - fibrosis, minimal - hyperplasia, acinar cell, focal, mild
		testes	- within normal limits
		tongue	- within normal limits
1121	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1121	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- hyperplasia, focal medullary, unilateral, mild - within normal limits - within normal limits

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1121	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - hydronephrosis, unilateral, mild - nephropathy, chronic progressive, bilateral, mild - pyelitis, unilateral, minimal - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1121	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric mammary gland nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland	- within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - dilatation, gland/lumen, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141

Dupont-18405-1238

H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1121	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1121	E	<b>Microscopic</b> tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1122	S	<b>Macroscopic</b> adrenal glands  kidneys lymph node, renal  skin	- mass, red, mass a, left, present approximately 2.2 x 2.0 x 1.0 cm. - cyst, clear, multiple, left, mild - within normal limits draining node for mass a, left. - nodule, tan, dorsal thoracic region, present corresponds to antemortem observation (nodule) approximately 0.4 cm in diameter.
1122	S	<b>Microscopic</b> adrenal glands	- pheochromocytoma, malignant, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (adrenal glands - mass a)

S - Scheduled necropsy  
E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1122	S	<b>Microscopic</b> kidneys	- cyst, unilateral, mild corresponds to macroscopic observation (kidneys - cyst) - nephropathy, chronic progressive, unilateral, mild one of pair present
		liver	- degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal
		lymph node, renal pancreas	- within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death
		skin	- hyperplasia, acinar cell, focal, minimal - keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin - nodule)
		testes tongue	- hyperplasia, interstitial cell, unilateral, minimal - within normal limits
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1123	S	<b>Macroscopic</b> lymph node, axillary  skin, subcutis	- within normal limits draining node for mass a, right. - mass, ulcerated, mass a, dorsal thoracic region, right, present corresponds to antemortem observation (nodule) approximately 2.5 x 1.0 x 2.0 cm, tan. - irregular surface, mild
1123	S	stomach, nonglandular <b>Microscopic</b> liver   lymph node, axillary pancreas	- degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, periportal, mild - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - atrophy, acinar, minimal - hyperplasia, acinar cell, focal, mild
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1123	S	<b>Microscopic</b> skin	- keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		stomach, nonglandular	- within normal limits
		testes	- within normal limits
		tongue	- within normal limits
		non-correlated macro observation	- stomach, nonglandular - irregular surface
1124	S	<b>Macroscopic</b> kidneys	- cyst, clear, right, mild
		lymph node, iliac	- enlarged, cystic, bilateral, moderate
		lymph node, inguinal	- within normal limits draining node for mass a, left.
		pituitary gland	- cyst, red, mild
		skin, subcutis	- mass, tan, mass a, left inguinal area, present approximately 1.5 x 1.0 x 1.0 cm.
		ureters	- distended with urine, bilateral, mild
		urinary bladder	- calculus/calculi, moderate
1124	S	<b>Microscopic</b> kidneys	- nephropathy, chronic progressive, unilateral, minimal

S - Scheduled necropsy

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1124	S	<b>Microscopic</b> liver	- hematopoiesis, extramedullary, minimal - vacuolation, periportal, minimal
		lymph node, iliac	- dilatation, sinus, mild corresponds to macroscopic observation (lymph node, iliac - enlarged)
		lymph node, inguinal	- within normal limits
		mammary gland	- adenoma, benign, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass a)
		pancreas	- atrophy, acinar, minimal - fibrosis, minimal
		pituitary gland	- hyperplasia, acinar cell, focal, mild - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - cyst)
		testes	- within normal limits
		tongue	- within normal limits
		ureters	- dilatation, bilateral, mild corresponds to macroscopic observation (ureters - distended with urine)
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1124	S	<b>Microscopic</b> urinary bladder	<ul style="list-style-type: none"> <li>- calculus/calculi, no grade corresponds to macroscopic observation (urinary bladder - calculus/calculi)</li> <li>- hyperplasia, papillary/nodular transitional cell, moderate corresponds to macroscopic observation (urinary bladder - calculus/calculi)</li> <li>- inflammation, mild</li> </ul>
1125	E	non-correlated macro observation  <b>Macroscopic</b> cavity, abdominal  lymph node, mesenteric  pancreas pituitary gland small intestine, jejunum	<ul style="list-style-type: none"> <li>- kidneys - cyst</li> <li>- adhesion, mild liver is adhered to the stomach.</li> <li>- enlarged, mild draining node for mass a.</li> <li>- edema, mild</li> <li>- enlarged, red, severe</li> <li>- mass, tan, mass a, present approximately 3.0 cm in diameter.</li> </ul>

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1125	E	<b>Macroscopic</b> spleen stomach, nonglandular thymus	- discoloration, tan, mild - laceration/perforation, moderate - cyst, clear, multiple, mild
1125	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain cavity, abdominal  coagulating glands epididymides esophagus	- vacuolation, focal, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - inflammation, acute, moderate corresponds to macroscopic observation (cavity, abdominal - adhesion) secondary to perforation of stomach by severe erosion/ulcer. - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1125	E	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - hyperplasia, transitional cell, unilateral, mild - nephropathy, chronic progressive, bilateral, severe - pyelitis, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - vacuolation, periportal, mild - metaplasia, osseous, minimal - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1125	E	<b>Microscopic</b> lymph node, mediastinal	- dilatation, sinus, moderate corresponds to macroscopic observation (thymus - cyst)
		lymph node, mesenteric	- dilatation, sinus, mild corresponds to macroscopic observation (lymph node, mesenteric - enlarged)
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		pancreas	- atrophy, acinar, minimal - inflammation, acute, mild corresponds to macroscopic observation (pancreas - edema)
		parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- inflammation, chronic-active, moderate

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1125	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum  spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen  stomach, glandular	- within normal limits - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - adenocarcinoma, malignant, primary, fatal, positive cause of death corresponds to macroscopic observation (small intestine, jejunum - mass a) - within normal limits - within normal limits - within normal limits - inflammation, peritoneal, mild corresponds to macroscopic observation (spleen - discoloration, tan) - gastropathy, uremic, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1125	E	<b>Microscopic</b> stomach, nonglandular	- erosion/ulcer, severe corresponds to macroscopic observation (stomach, nonglandular - laceration/perforation)
		testes	- within normal limits
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- inflammation, minimal
		Cause of Death	- gastrointestinal tumor
1126	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1126	E	<b>Microscopic</b> adrenal glands	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - vacuolation, focal, unilateral, mild

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1126	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, bilateral, mild - cardiomyopathy, minimal - within normal limits - hydronephrosis, unilateral, mild - nephropathy, chronic progressive, bilateral, mild - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1126	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	- within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1126	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1126	E	<b>Microscopic</b> stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - dilatation, unilateral, mild - within normal limits - pituitary tumor
1127	S	<b>Macroscopic</b> kidneys  lymph node, inguinal  mammary gland pituitary gland	- enlarged, left, severe irregular surface and yellow. - not identified, right, no grade draining node for mass a. - swollen/thickened, generalized, mild - focus/foci, black, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1127	S	<b>Macroscopic</b> skin, subcutis	- mass, ulcerated, mass a, dorsal thoracic region, present corresponds to antemortem observation (nodule hair sparse) approximately 2.0 cm in diameter, tan.
1127	S	<b>Microscopic</b> kidneys	- carcinoma, tubular cell, malignant, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (kidneys - enlarged)
		liver	- degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, focal, minimal
		mammary gland	- hyperplasia, lobular, mild corresponds to macroscopic observation (mammary gland - swollen/thickened)
		pancreas	- hyperplasia, acinar cell, focal, mild
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - focus/foci, black)
S - Scheduled necropsy			

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1127	S	<b>Microscopic</b> skin	- keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		testes	- within normal limits
		tongue	- within normal limits
1128	E	<b>Macroscopic</b> lymph node, mandibular	- within normal limits draining node for mass a, left.
		pituitary gland	- enlarged, red, moderate
		skeletal muscle	- mass, tan, mass a, left lateral head, present corresponds to antemortem observation (swelling) approximately 3.5 cm in diameter, temporal muscle.
1128	E	<b>Microscopic</b> adrenal glands	- hyperplasia, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone	- osteosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skeletal muscle - mass a)
		bone marrow, femur	- within normal limits

S - Scheduled necropsy  
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MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1128	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - mesothelioma, malignant, bilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - pyelitis, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1128	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	 - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, periportal, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1128	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- inflammation, acute, minimal
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1128	E	<b>Microscopic</b> stomach, nonglandular testes  thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - hyperplasia, interstitial cell, unilateral, minimal - mesothelioma, malignant, unilateral, secondary - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1129	E	<b>Macroscopic</b> pituitary gland	- enlarged, severe
1129	E	<b>Microscopic</b> adrenal glands  aorta	- hyperplasia, focal medullary, unilateral, minimal - vacuolation, focal, unilateral, minimal - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1129	E	<b>Microscopic</b> bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, mild - within normal limits - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1129	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland	- within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - inflammation, subacute/chronic, minimal - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - exudate, nasal passage, mild - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141

Dupont-18405-1238

H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1129	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes	 - within normal limits - atrophy, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, epithelial, nonglandular, mild - inflammation, mild - adenoma, interstitial cell, benign, unilateral, primary, incidental, not cause of death - hyperplasia, interstitial cell, bilateral, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1129	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1130	E	<b>Macroscopic</b> lymph node, axillary  pituitary gland skin	- within normal limits draining node for mass a, right. - enlarged, red, mild - abrasion/scab, red, dorsal thoracic region, left, mild corresponds to antemortem observation (scabbed area) - mass, tan, mass a, dorsal thoracic region, present corresponds to antemortem observation (nodule) approximately 1.5 cm in diameter.

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1130	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- angiectasis/cystic degeneration, focal cortical, bilateral, mild - hyperplasia, focal cortical, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1130	E	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, mild - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal - within normal limits - dilatation, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1130	E	<b>Microscopic</b> parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin - abrasion/scab; skin - mass a) both skin observations appear to be the same lesion.
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1130	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - astrocytoma, malignant, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - adenoma, follicular cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - spinal cord tumor

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1131	D	<b>Macroscopic</b> lymph node, hepatic skin small intestine, jejunum tongue	- enlarged, tan, moderate - absent portion/cannibalized, nose/muzzle, no grade - impacted, mild - absent portion/cannibalized, no grade
1131	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1131	D	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys  lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular	- within normal limits - within normal limits - cardiomyopathy, moderate - within normal limits - mineralization, tubular, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infarct, severe corresponds to macroscopic observation (lymph node, hepatic - enlarged) a severely infarcted liver lobe which has been surrounded by a fibrotic capsule. no hepatic lymph node present. - vacuolation, diffuse, mild - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1131	D	<b>Microscopic</b> lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - cyst, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1131	D	<b>Microscopic</b> small intestine, ileum small intestine, jejunum  spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - dilatation, gland/lumen, moderate corresponds to macroscopic observation (small intestine, jejunum - impacted) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - liver inflammation/necrosis

D - Died on Study



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1132	S	<b>Macroscopic</b> bone, femur	- irregular surface, left, moderate head expanded and irregular. same change in acetabulum.
1132	S	<b>Microscopic</b> bone, femur	- osteoarthritis/pododermatitis, moderate corresponds to macroscopic observation (bone, femur - irregular surface)
		liver	- hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, periportal, minimal
		pancreas	- atrophy, acinar, minimal
		testes	- within normal limits
		tongue	- within normal limits
		non-correlated macro observation	- bone, femur - irregular surface
1133	D	<b>Macroscopic</b> all tissues	- within normal limits
1133	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, mild

S - Scheduled necropsy  
D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1133	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - polyarteritis, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1133	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx  liver  lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b  nose, level c	- within normal limits - within normal limits - foreign material, moderate plant. - infiltration, mononuclear cell, minimal - vacuolation, centrilobular, minimal - bacterial colonies, minimal - foreign material, minimal plant. - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - foreign material, mild plant. - exudate, nasal passage, minimal - foreign material, minimal plant.
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1133	D	<b>Microscopic</b> nose, level d  pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- foreign material, minimal plant. - polyarteritis, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1133	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - aspiration of foreign material
1134	E	<b>Macroscopic</b> foot/feet	- ulcer, plantar/palmar, red, severe corresponds to antemortem observation (nodule)
1134	E	<b>Microscopic</b> adrenal glands	- hypertrophy, focal cortical, unilateral, minimal - vacuolation, focal, unilateral, minimal

E - Euthanized *in extremis*  
D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1134	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides  esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - granuloma, spermatic, unilateral, moderate - oligospermia/germ cell debris, unilateral, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1134	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	- within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1134	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, mild
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1134	E	<b>Microscopic</b> testes  thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- adenoma, interstitial cell, benign, unilateral, primary, incidental, not cause of death - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - osteoarthritis/pododermatitis
1135	D	<b>Macroscopic</b> kidneys lung with bronchi pituitary gland skin	- cyst, clear, multiple, right, moderate - focus/foci, white, multiple lobes, mild - enlarged, mild - hair sparse, left foreleg/limb, moderate corresponds to antemortem observation (hair sparse)
1135	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, minimal
E - Euthanized <i>in extremis</i> D - Died on Study			

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1135	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - cyst, unilateral, mild corresponds to macroscopic observation (kidneys - cyst) - nephropathy, chronic progressive, bilateral, severe
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1135	D	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal corresponds to macroscopic observation (lung with bronchi - focus/foci, white) - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1135	D	<b>Microscopic</b> pancreas	- atrophy, acinar, minimal - carcinoma, islet cell, malignant, primary, incidental, not cause of death - hyperplasia, acinar cell, focal, minimal
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- alopecia/hypotrichosis, mild corresponds to macroscopic observation (skin - hair sparse)
		small intestine, duodenum	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1135	D	<b>Microscopic</b> small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - polyarteritis, bilateral, mild - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1136	E	<b>Macroscopic</b> lymph node, iliac pituitary gland	- enlarged, bilateral, mild - enlarged, red, severe
1136	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands  epididymides esophagus eyes eyes, optic nerves eyes, retina galt	- angiectasis/cystic degeneration, focal cortical, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - inflammation, unilateral, moderate one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1136	E	<b>Microscopic</b> harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, iliac  lymph node, mandibular lymph node, mesenteric nerve, sciatic	- within normal limits - cardiomyopathy, mild - within normal limits - hyperplasia, transitional cell, bilateral, mild - nephropathy, chronic progressive, bilateral, mild - pyelonephritis, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - within normal limits - dilatation, sinus, moderate corresponds to macroscopic observation (lymph node, iliac - enlarged) - within normal limits - within normal limits - degeneration, axonal/myelin, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1136	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - inflammation, subacute/chronic, moderate - within normal limits - within normal limits - within normal limits - inflammation, bilateral, severe - within normal limits - within normal limits

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1136	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder  Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, c-cell, focal, unilateral, moderate - within normal limits - within normal limits - within normal limits - hyperplasia, simple transitional cell, mild - inflammation, minimal - pituitary tumor

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1137	D	<b>Macroscopic</b> tongue	- absent portion/cannibalized, no grade corresponds to antemortem observation (cannibalized/partially cannibalized)
1137	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis
D - Died on Study			

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1137	D	<b>Microscopic</b> galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	- not examined - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - bacterial colonies, mild large area with lysis of red blood cells indicative of dosing injury. - within normal limits - not examined - degeneration, axonal/myelin, minimal - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1137	D	<b>Microscopic</b> nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar	 - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1137	D	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1138	E	<b>Macroscopic</b> eyes  kidneys	- cloudy, bilateral, moderate corresponds to antemortem observation (eye discolored) - dilatation, pelvic, right, mild
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1138	E	<b>Macroscopic</b> lymph node, mandibular  skin, subcutis	- within normal limits draining node for mass a, bilateral. - mass, tan, mass a, ventral neck, present corresponds to antemortem observation (mass 1) approximately 9.7 x 9.0 x 4.5 cm. - irregular surface, tan, mucosa, mild
1138	E	stomach, glandular <b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1138	E	<b>Microscopic</b> eyes  eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- cataract, bilateral, moderate corresponds to macroscopic observation (eyes - cloudy) - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - vacuolation, focal, minimal - histiocytosis, alveolar, minimal
E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1138	E	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - degeneration, axonal/myelin, mild - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal - within normal limits
E - Euthanized <i>in extremis</i>			



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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1138	E	<b>Microscopic</b> skin, subcutis	- fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		testes	- within normal limits
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- hyperplasia, c-cell, focal, unilateral, minimal
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1138	E	<b>Microscopic</b> non-correlated macro observation	- kidneys - dilatation, pelvic - stomach, glandular - irregular surface
		Cause of Death	- fibrosarcoma/fibroma
1139	D	<b>Macroscopic</b> tongue	- absent/cannibalized, no grade portion of tip of tongue absent.
1139	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1139	D	<b>Microscopic</b> esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - bacterial colonies, minimal - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1139	D	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1139	D	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - probable dosing injury
1140	S	<b>Macroscopic</b> lymph node, mesenteric	- enlarged, mild

S - Scheduled necropsy  
D - Died on Study

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1140	S	<b>Macroscopic</b> small intestine, jejunum	- enlarged, red, moderate
1140	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, focal, minimal
		lymph node, mesenteric	- dilatation, sinus, mild corresponds to macroscopic observation (lymph node, mesenteric - enlarged)
		pancreas	- hyperplasia, acinar cell, focal, minimal
		small intestine, jejunum	- erosion/ulcer, severe corresponds to macroscopic observation (small intestine, jejunum - enlarged) - lymphangiectasis, mild corresponds to macroscopic observation (small intestine, jejunum - enlarged)
		testes	- within normal limits
		tongue	- within normal limits
S - Scheduled necropsy			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1141	D	<b>Macroscopic</b> pituitary gland	- enlarged, red, moderate
1141	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain  coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - hemorrhage, mild - within normal limits - oligospermia/germ cell debris, unilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1141	D	<b>Microscopic</b> heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands	 - within normal limits - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1141	D	<b>Microscopic</b> pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic	- within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) severe hemorrhage. - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1141	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - degeneration/atrophy, seminiferous tubules, unilateral, moderate - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - accidental injury
1142	D	<b>Macroscopic</b> all tissues	- within normal limits
1142	D	<b>Microscopic</b> adrenal glands	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - vacuolation, focal, unilateral, minimal
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1142	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1142	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx  liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx	- within normal limits - within normal limits - exudate, luminal, minimal - foreign material, mild plant material. - inflammation, minimal - infiltration, mononuclear cell, minimal - granuloma, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present - within normal limits
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1142	D	<b>Microscopic</b> pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1142	D	<b>Microscopic</b> thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1143	S	<b>Macroscopic</b> kidneys liver  lymph node, hepatic	- irregular surface, bilateral, mild - mass, tan, mass a, median lobe, present approximately 3.0 cm in diameter. - within normal limits draining node for mass a.
1143	S	<b>Microscopic</b> kidneys	- hydronephrosis, bilateral, mild - nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface)
S - Scheduled necropsy D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1143	S	<b>Microscopic</b> liver	- adenoma, hepatocellular, benign, primary, incidental, not cause of death corresponds to macroscopic observation (liver - mass a) - degeneration, cystic, focal, minimal - focus of cellular alteration, clear, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal
		lymph node, hepatic	- within normal limits
		pancreas	- within normal limits
		testes	- dilatation, seminiferous tubules, bilateral, minimal - polyarteritis, bilateral, mild
		tongue	- within normal limits
1144	D	<b>Macroscopic</b> all tissues	- within normal limits
1144	D	<b>Microscopic</b> adrenal glands	- within normal limits

S - Scheduled necropsy  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1144	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits
D - Died on Study			



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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1144	D	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - bacterial colonies, mild extensive areas with lysis of red blood cells indicative of dosing injury. - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1144	D	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		testes	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1144	D	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1145	E	<b>Macroscopic</b> foot/feet	- enlarged, left hindleg/limb, mild corresponds to antemortem observation (swelling)
1145	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1145	E	<b>Microscopic</b> bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart hind limb/leg  joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - inflammation, moderate corresponds to macroscopic observation (foot/feet - enlarged) - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1145	E	<b>Microscopic</b> larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid	- within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, acinar cell, benign, primary, incidental, not cause of death - polyarteritis, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1145	E	<b>Microscopic</b> salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1145	E	<b>Microscopic</b> urinary bladder Cause of Death	- within normal limits - inflammation/septicemia
1146	D	<b>Macroscopic</b> pituitary gland	- enlarged, red, mild
1146	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1146	D	<b>Microscopic</b> eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric	- within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - fibrosis, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1146	D	<b>Microscopic</b> nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1146	D	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1147	S	<b>Macroscopic</b> all tissues	- within normal limits
1147	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - vacuolation, focal, minimal
		pancreas	- within normal limits
		testes	- within normal limits
		tongue	- within normal limits
1148	E	<b>Macroscopic</b> foot/feet	- absent, portion, left hindleg/limb, digit, no grade corresponds to antemortem observation (swelling)
		testes	- focus/foci, tan, left, mild
1148	E	<b>Microscopic</b> adrenal glands	- within normal limits

S - Scheduled necropsy  
E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1148	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - astrocytoma, malignant, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1148	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands	 - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, minimal - vacuolation, periportal, minimal - within normal limits - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - exudate, nasal passage, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1148	E	<b>Microscopic</b> pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1148	E	<b>Microscopic</b> testes	- adenoma, interstitial cell, benign, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (testes - focus/foci, tan)
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		Cause of Death	- brain tumor
1149	E	<b>Macroscopic</b> lymph node, inguinal	- not identified, no grade draining node for mass a.
		skin, subcutis	- mass, tan, mass a, right inguinal area, present corresponds to antemortem observation (mass 1) approximately 9.0 cm in diameter.
1149	E	<b>Microscopic</b> adrenal glands	- hypertrophy, focal cortical, unilateral, minimal

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1149	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - astrocytoma, malignant, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*



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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1149	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland prostate gland	 - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, minimal - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, pars distalis, mild - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1149	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - lipoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1149	E	<b>Microscopic</b> thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - lipoma/liposarcoma
1150	S	<b>Macroscopic</b> all tissues	- within normal limits
1150	S	<b>Microscopic</b> liver  pancreas testes tongue	- focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - hyperplasia, acinar cell, focal, minimal - hyperplasia, interstitial cell, unilateral, minimal - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141

Dupont-18405-1238

H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1151	E	<b>Macroscopic</b> pituitary gland	- enlarged, tan, severe
1151	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1151	E	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands	- within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1151	E	<b>Microscopic</b> pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration/regeneration, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1151	E	<b>Microscopic</b> stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1152	E	<b>Macroscopic</b> pituitary gland stomach, nonglandular	- enlarged, red, severe - focus/foci, tan, mild - irregular surface, serosa, mild
1152	E	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, minimal - vacuolation, focal, unilateral, minimal

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1152	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits

E - Euthanized *in extremis*



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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1152	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx	 - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - vacuolation, periportal, moderate - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1152	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- inflammation, unilateral, minimal
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1152	E	<b>Microscopic</b> stomach, nonglandular	- erosion/ulcer, severe corresponds to macroscopic observation (stomach, nonglandular - focus/foci, tan; stomach, nonglandular - irregular surface)
		testes	- within normal limits
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		Cause of Death	- pituitary tumor
1153	E	<b>Macroscopic</b> eyes	- cloudy, bilateral, moderate corresponds to antemortem observation (eye discolored)
		foot/feet	- swollen/thickened, left hindleg/limb, mild corresponds to antemortem observation (swelling)
1153	E	<b>Microscopic</b> adrenal glands	- within normal limits

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1153	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes  eyes, optic nerves eyes, retina foot/feet galt harderian glands heart joint, tibiofemoral	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cataract, bilateral, moderate corresponds to macroscopic observation (eyes - cloudy) - within normal limits - within normal limits - inflammation, unilateral, moderate - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits

E - Euthanized *in extremis*

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1153	E	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- cyst, unilateral, mild - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal - macrophages, pigmented alveolar, minimal - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - inflammation, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1153	E	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	 - hyperplasia, acinar cell, focal, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1153	E	<b>Microscopic</b> stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - foot/feet; inflammation; unilateral, moderate
1154	S	<b>Macroscopic</b> pituitary gland prostate gland urinary bladder	- enlarged, minimal - focus/foci, yellow, mild - calculus/calculi, moderate
1154	S	<b>Microscopic</b> liver pancreas	- hematopoiesis, extramedullary, minimal - within normal limits
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1154	S	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- inflammation, chronic-active, severe corresponds to macroscopic observation (prostate gland - focus/foci, yellow)
		testes	- within normal limits
		tongue	- within normal limits
		urinary bladder	- calculus/calculi, no grade corresponds to macroscopic observation (urinary bladder - calculus/calculi) - hyperplasia, papillary/nodular transitional cell, moderate corresponds to macroscopic observation (urinary bladder - calculus/calculi) - inflammation, mild
S - Scheduled necropsy			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1155	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, bilateral.
		skin, subcutis	- mass, scabbed, mass a, dorsal thoracic region, present corresponds to antemortem observation (nodule scabbed area) approximately 4.0 cm in diameter, tan.
1155	E	<b>Microscopic</b> adrenal glands	- within normal limits
		aorta	- within normal limits
		bone marrow, femur	- hyperplasia, mixed, mild
		bone marrow, sternum	- hyperplasia, mixed, mild
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1155	E	<b>Microscopic</b> eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	 - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1155	E	<b>Microscopic</b> nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin  small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, squamous cell, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1155	E	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - skin tumor
1156	E	<b>Macroscopic</b> lacrimal glands, exorbital	- not identified, right, no grade

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1156	E	<b>Macroscopic</b> lymph node, axillary  skin, subcutis	- within normal limits right is draining node for mass a. - mass, tan, mass a, right lateral neck, present corresponds to antemortem observation (mass 1) approximately 6.0 x 6.0 x 5.0 cm and encompasses the right forelimb and shoulder.
1156	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes	- hyperplasia, focal cortical, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1156	E	<b>Microscopic</b> eyes, optic nerves eyes, retina gall harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital  large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - hemangiosarcoma, malignant, secondary
E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1156	E	<b>Microscopic</b> lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular	- erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - atrophy, acinar, minimal - fibrosis, minimal - hyperplasia, acinar cell, focal, mild - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1156	E	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes thymus	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hemangiosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - hyperplasia, epithelial, nonglandular, moderate - inflammation, mild - within normal limits - depletion, lymphoid, generalized, moderate

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1156	E	<b>Microscopic</b> thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hemangiosarcoma/hemangioma
1157	E	<b>Macroscopic</b> adipose tissue  kidneys liver pituitary gland prostate gland stomach, glandular testes	- focus/foci, yellow, minimal white fat near epididymis. - irregular surface, bilateral, minimal - focus/foci, tan, multiple lobes, mild - enlarged, red, severe - enlarged, tan, mild - focus/foci, tan, mucosa, mild - small, bilateral, mild
1157	E	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, minimal

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1157	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - inflammation, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface) - pyelitis, bilateral, minimal

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1157	E	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric mesentery/peritoneum  nerve, sciatic nose, level a nose, level b nose, level c	- within normal limits - within normal limits - within normal limits - inflammation, peritoneal, mild - within normal limits - necrosis, focal, severe corresponds to macroscopic observation (liver - focus/foci, tan) consistent with infarcts. - vacuolation, periportal, mild - within normal limits - within normal limits - within normal limits - necrosis, fat, mild corresponds to macroscopic observation (adipose tissue - focus/foci, yellow) - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1157	E	<b>Microscopic</b> nose, level d pancreas  parathyroid glands  pharynx pituitary gland  prostate gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- within normal limits - atrophy, acinar, minimal - hyperplasia, acinar cell, focal, mild - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - inflammation, acute, severe corresponds to macroscopic observation (prostate gland - enlarged) - within normal limits - within normal limits - within normal limits - inflammation, bilateral, minimal - degeneration/necrosis, myofiber, mild - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1157	E	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen  stomach, glandular  stomach, nonglandular testes  thymus thyroid gland  tongue trachea	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hemangiosarcoma, malignant, primary, incidental, not cause of death - erosion/ulcer, moderate corresponds to macroscopic observation (stomach, glandular - focus/foci, tan) - erosion/ulcer, mild - degeneration/atrophy, seminiferous tubules, bilateral, mild corresponds to macroscopic observation (testes - small) - depletion, lymphoid, generalized, severe - adenoma, c-cell, benign, bilateral, primary, incidental, not cause of death - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1157	E	<b>Microscopic</b> ureters urinary bladder  Cause of Death	- within normal limits - hyperplasia, simple transitional cell, minimal - inflammation, moderate - liver inflammation/necrosis
1158	E	<b>Macroscopic</b> tail	- focus/foci, tan, moderate corresponds to antemortem observation (ulcer scabbed area) ulcer approximately 2.0 x 1.0 cm.
1158	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur	- hyperplasia, focal cortical, bilateral, minimal - hyperplasia, focal medullary, unilateral, minimal - vacuolation, focal, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1158	E	<b>Microscopic</b> bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - pyelitis, unilateral, minimal  - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1158	E	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal
		lung	- adenocarcinoma (primary site unknown), malignant, primary, incidental, not cause of death
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		nerve, sciatic	- degeneration, axonal/myelin, minimal
		nose, level a	- inflammation, minimal
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death
		parathyroid glands	- hyperplasia, focal, unilateral, minimal
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1158	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular tail  testes	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - erosion/ulcer, severe corresponds to macroscopic observation (tail - focus/foci, tan) - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1158	E	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, moderate
			- hyperplasia, epithelial cell, minimal
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		Cause of Death	- tail; erosion/ulcer; severe
1159	E	<b>Macroscopic</b> adrenal glands	- enlarged, left, mild
		kidneys	- irregular surface, bilateral, mild
		stomach, nonglandular	- swollen/thickened, mild
1159	E	<b>Microscopic</b> adrenal glands	- pheochromocytoma, benign, bilateral, primary, incidental, not cause of death
			corresponds to macroscopic observation (adrenal glands - enlarged)
		aorta	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141

Dupont-18405-1238

H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1159	E	<b>Microscopic</b> bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes  eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral	 - within normal limits - within normal limits - within normal limits - within normal limits - astrocytoma, malignant, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - metaplasia, squamous, bilateral, minimal - neovascularization, corneal, bilateral, mild - within normal limits - within normal limits - within normal limits - hyperplasia, focal, bilateral, minimal - cardiomyopathy, mild - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141

Dupont-18405-1238

H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1159	E	<b>Microscopic</b> kidneys	<ul style="list-style-type: none"><li>- hydronephrosis, bilateral, minimal</li><li>- hyperplasia, transitional cell, unilateral, minimal</li><li>- nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface)</li></ul>
		lacrimal glands, exorbital	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		large intestine, cecum	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		large intestine, colon	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		large intestine, rectum	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		larynx	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		liver	<ul style="list-style-type: none"><li>- hyperplasia, bile duct, minimal</li><li>- infiltration, mononuclear cell, minimal</li></ul>
		lung	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		lymph node, mandibular	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		lymph node, mesenteric	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		nerve, sciatic	<ul style="list-style-type: none"><li>- degeneration, axonal/myelin, minimal</li></ul>
		nose, level a	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		nose, level b	<ul style="list-style-type: none"><li>- within normal limits</li></ul>
		nose, level c	<ul style="list-style-type: none"><li>- within normal limits</li></ul>

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1159	E	<b>Microscopic</b> nose, level d pancreas  parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical	- within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - adenoma, benign, unilateral, primary, incidental, not cause of death - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, mild - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1159	E	<b>Microscopic</b> spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, moderate corresponds to macroscopic observation (stomach, nonglandular - swollen/thickened) - within normal limits - depletion, lymphoid, generalized, severe - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - brain tumor
1160	D	<b>Macroscopic</b> adrenal glands	- small, right, moderate

E - Euthanized *in extremis*  
D - Died on Study

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u>			
1160	D	<b>Macroscopic</b> pituitary gland	- enlarged, severe
1160	D	<b>Microscopic</b> adrenal glands	- atrophy, cortical, unilateral, moderate corresponds to macroscopic observation (adrenal glands - small) one medulla present
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), mild
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1160	D	<b>Microscopic</b> harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c	- within normal limits - cardiomyopathy, mild - within normal limits - cyst, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1160	D	<b>Microscopic</b> nose, level d pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits - hyperplasia, acinar cell, focal, moderate - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>0.1 mg/kg/day</u> 1160	D	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hypertrophy/hyperplasia, follicular cell, bilateral, moderate - inflammation, subacute/chronic, bilateral, mild inflammation is located on the external surface of the gland. - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1171	S	<b>Macroscopic</b> pituitary gland seminal vesicles stomach, glandular	- enlarged, severe - small, bilateral, severe - swollen/thickened, mucosa, mild
1171	S	<b>Microscopic</b> coagulating glands liver pancreas pituitary gland  seminal vesicles  stomach, glandular testes tongue non-correlated macro observation	- depletion, secretory, bilateral, severe - hematopoiesis, extramedullary, minimal - atrophy, acinar, minimal - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - depletion, secretory, bilateral, severe corresponds to macroscopic observation (seminal vesicles - small) - within normal limits - degeneration/atrophy, seminiferous tubules, bilateral, mild - within normal limits - stomach, glandular - swollen/thickened
S - Scheduled necropsy			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1172	E	<b>Macroscopic</b> pituitary gland	- enlarged, red, severe
1172	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1172	E	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1172	E	<b>Microscopic</b> pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical	- within normal limits - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1172	E	<b>Microscopic</b> spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1173	E	<b>Macroscopic</b> aorta kidneys	- discoloration, gray, mild - irregular surface, bilateral, moderate

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1173	E	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, right.
		pituitary gland	- enlarged, severe
		skin, subcutis	- mass, tan, mass a, right axillary area, present corresponds to antemortem observation (mass 1) approximately 3.0 cm in diameter.
1173	E	stomach, glandular testes	- swollen/thickened, mucosa, moderate - small, bilateral, mild
		<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, unilateral, minimal - pheochromocytoma, benign, bilateral, primary, incidental, not cause of death
		aorta	- vacuolation, focal, unilateral, minimal - mineralization, severe corresponds to macroscopic observation (aorta - discoloration, gray)
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits

E - Euthanized *in extremis*



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1173	E	<b>Microscopic</b> bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart  joint, tibiofemoral	- fibrous osteodystrophy, moderate - fibrous osteodystrophy, mild - within normal limits - inflammation, bilateral, moderate - oligospermia/germ cell debris, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, moderate - mineralization, vascular, mild - within normal limits
E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1173	E	<b>Microscopic</b> kidneys	<ul style="list-style-type: none"> <li>- hyperplasia, transitional cell, bilateral, mild</li> <li>- mineralization, tubular, bilateral, mild</li> <li>- mineralization, vascular, bilateral, minimal</li> <li>- nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface)</li> <li>- thrombus, bilateral, moderate renal vein. secondary to severe nephropathy.</li> </ul>
		lacrimal glands, exorbital	- within normal limits
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- hyperplasia, bile duct, mild
		lung	- pneumonitis, uremic, moderate
		lymph node, axillary	- within normal limits
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		nerve, sciatic	- degeneration, axonal/myelin, minimal

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1173	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- fibrous osteodystrophy, moderate - fibrous osteodystrophy, moderate - fibrous osteodystrophy, moderate - fibrous osteodystrophy, moderate - fibrosis, minimal - mineralization, vascular, mild - hyperplasia, diffuse, bilateral, moderate - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - mineralization, vascular, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1173	E	<b>Microscopic</b> skin, subcutis	- abscess, moderate corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, mild
		stomach, glandular	- gastropathy, uremic, moderate corresponds to macroscopic observation (stomach, glandular - swollen/thickened)
		stomach, nonglandular	- gastropathy, uremic, mild
		testes	- degeneration/atrophy, seminiferous tubules, bilateral, moderate corresponds to macroscopic observation (testes - small)
			- polyarteritis, bilateral, minimal
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- within normal limits
		tongue	- mineralization, vascular, minimal

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1173	E	<b>Microscopic</b> trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - chronic progressive nephropathy/uremia
1174	D	<b>Macroscopic</b> cavity, thoracic  prostate gland	- fluid, red, mild approximately 5.0 ml. - discoloration, tan, moderate
1174	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1174	D	<b>Microscopic</b> coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart  joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - endocarditis, valvular vegetative, moderate - within normal limits - inflammation, chronic-active, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - leukocytosis, sinusoidal, minimal - leukocytosis, vascular, mild
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1174	D	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland  salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present - within normal limits - within normal limits - inflammation, acute, severe corresponds to macroscopic observation (prostate gland - discoloration, tan) - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1174	D	<b>Microscopic</b> skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - heart inflammation/necrosis
D - Died on Study			



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1175	D	<b>Macroscopic</b> all tissues	- within normal limits
1175	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1175	D	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx  liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	- within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - exudate, luminal, minimal - mucus increased, minimal - focus of cellular alteration, basophilic, minimal - focus of cellular alteration, clear, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, focal, minimal - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1175	D	<b>Microscopic</b> nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar	 - within normal limits - within normal limits - atrophy, acinar, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1175	D	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1176	S	<b>Macroscopic</b> lymph node, inguinal  lymph node, mesenteric pituitary gland	- within normal limits draining node for mass a and mass b, left. - enlarged, red, mild - enlarged, severe

S - Scheduled necropsy  
D - Died on Study

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1176	S	<b>Macroscopic</b> skin, subcutis	<ul style="list-style-type: none"> <li>- mass, tan, mass a, left ventral abdomen, present approximately 1.0 cm in diameter.</li> <li>- mass, tan, mass b, left ventral abdomen, present approximately 1.0 cm in diameter.</li> <li>- enlarged, right, mild</li> </ul>
1176	S	thyroid gland <b>Microscopic</b> liver	<ul style="list-style-type: none"> <li>- degeneration, cystic, focal, minimal</li> <li>- hematopoiesis, extramedullary, minimal</li> <li>- hyperplasia, bile duct, minimal</li> <li>- vacuolation, periportal, minimal</li> </ul>
		lymph node, inguinal lymph node, mesenteric	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- hemangiosarcoma, malignant, primary, incidental, not cause of death</li> <li>- corresponds to macroscopic observation (lymph node, mesenteric - enlarged)</li> </ul>
		pancreas	<ul style="list-style-type: none"> <li>- atrophy, acinar, minimal</li> <li>- hyperplasia, acinar cell, focal, mild</li> </ul>
S - Scheduled necropsy			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1176	S	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		skin	- carcinoma, squamous cell, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass a)
		skin, subcutis	- fibroma, benign, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass b)
		testes	- within normal limits
		thyroid gland	- adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death corresponds to macroscopic observation (thyroid gland - enlarged)
		tongue	- within normal limits
1177	D	<b>Macroscopic</b> all tissues	- within normal limits

S - Scheduled necropsy  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1177	D	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- within normal limits one medulla present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits
D - Died on Study			

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1177	D	<b>Microscopic</b> lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - necrosis, hepatocytes, centrilobular, severe - within normal limits - within normal limits - within normal limits - within normal limits - exudate, nasal passage, minimal - exudate, nasal passage, minimal - fungus/yeast, moderate - inflammation, acute, minimal - metaplasia, squamous, minimal
D - Died on Study			



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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1177	D	<b>Microscopic</b> nose, level c	- erosion/ulcer, mild - exudate, nasal passage, mild - fungus/yeast, severe - inflammation, acute, minimal - metaplasia, squamous, mild
		nose, level d	- erosion/ulcer, moderate - inflammation, acute, mild - metaplasia, squamous, mild
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- within normal limits
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1177	D	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - nose/oral inflammation/ulceration
D - Died on Study			

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1178	S	<b>Macroscopic</b> lymph node, inguinal  pituitary gland skin, subcutis	- within normal limits draining node for mass a, right. - enlarged, red, mild - mass, tan, mass a, right inguinal area, present corresponds to antemortem observation (mass 1) approximately 3.5 cm in diameter. - nodule, tan, ventral neck, left, present corresponds to antemortem observation (nodule) approximately 0.4 cm in diameter.
1178	S	<b>Microscopic</b> liver  lymph node, inguinal pancreas  pituitary gland	- hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - within normal limits - atrophy, acinar, minimal - polyarteritis, moderate - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
S - Scheduled necropsy			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1178	S	<b>Microscopic</b> skin  skin, subcutis  testes tongue	- cyst, keratin, mild corresponds to macroscopic observation (skin, subcutis - nodule) - fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits
1179	D	<b>Macroscopic</b> all tissues	- within normal limits
1179	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

S - Scheduled necropsy  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1179	D	<b>Microscopic</b> coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver	- within normal limits - within normal limits - within normal limits - hemorrhage, unilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - mucus increased, mild - infiltration, mononuclear cell, minimal - vacuolation, centrilobular, minimal
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1179	D	<b>Microscopic</b> lung	- bacterial colonies, minimal - mucus increased, mild small areas of red blood cell lysis.
		lymph node, mandibular	- within normal limits
		lymph node, mesenteric	- within normal limits
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1179	D	<b>Microscopic</b> seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - bacterial colonies, minimal - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1179	D	<b>Microscopic</b> Cause of Death	- dosing injury
1180	S	<b>Macroscopic</b> lymph node, mandibular  skin, subcutis	- within normal limits draining node for mass a, right. - mass, tan, mass a, right lateral neck, present approximately 1.5 cm in diameter.
1180	S	<b>Microscopic</b> liver lymph node, mandibular mammary gland  pancreas testes tongue	- hematopoiesis, extramedullary, minimal - within normal limits - fibroadenoma, benign, primary, incidental, not cause of death corresponds to macroscopic observation (skin, subcutis - mass a) - hyperplasia, acinar cell, focal, moderate - within normal limits - within normal limits
S - Scheduled necropsy D - Died on Study			



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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1181	D	<b>Macroscopic</b> eyes eyes, optic nerves eyes, retina harderian glands lacrimal glands, exorbital tongue	- absent/cannibalized, bilateral, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, bilateral, no grade - absent/cannibalized, right, no grade - absent/cannibalized, right, no grade - absent portion/cannibalized, no grade
1181	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1181	D	<b>Microscopic</b> eyes, optic nerves	- not examined cannibalized
		eyes, retina	- not examined
		galt	- within normal limits
		harderian glands	- within normal limits one of pair present
		heart	- within normal limits
		joint, tibiofemoral	- within normal limits
		kidneys	- within normal limits
		lacrimal glands, exorbital	- within normal limits one of pair present one cannibalized.
		large intestine, cecum	- within normal limits
		large intestine, colon	- within normal limits
		large intestine, rectum	- within normal limits
		larynx	- within normal limits
		liver	- within normal limits
		lung	- bacterial colonies, minimal red blood cell lysis.

D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1181	D	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1181	D	<b>Microscopic</b> small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1182	D	<b>Macroscopic</b> all tissues	- within normal limits
1182	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart	- hyperplasia, focal cortical, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal
D - Died on Study			

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Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1182	D	<b>Microscopic</b> joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - angiectasis, minimal - focus of cellular alteration, basophilic, minimal - hyperplasia, bile duct, minimal - vacuolation, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1182	D	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- fibrosis, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1182	D	<b>Microscopic</b> stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1183	D	<b>Macroscopic</b> lymph node, axillary  skin, subcutis	- within normal limits draining node for mass a, right. - mass, ulcerated, mass a, right axillary area, present corresponds to antemortem observation (nodule) approximately 1.0 cm in diameter, tan.
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1183	D	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1183	D	<b>Microscopic</b> lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, clear, minimal - infiltration, mononuclear cell, minimal - vacuolation, periportal, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, mild
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1183	D	<b>Microscopic</b> parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- adenoma, basal cell, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1183	D	<b>Microscopic</b> spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder Cause of Death	- hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - carcinoma, follicular cell, malignant, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - skin tumor
1184	E	<b>Macroscopic</b> lymph node, axillary  pituitary gland	- within normal limits draining node for mass a, left. - enlarged, red, severe

E - Euthanized *in extremis*  
D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1184	E	<b>Macroscopic</b> skin, subcutis	- mass, tan, mass a, left axillary area, present corresponds to antemortem observation (nodule swelling) approximately 7.0 x 7.0 x 2.0 cm.
1184	E	stomach, glandular <b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves	- irregular surface, mucosa, mild  - hyperplasia, focal cortical, unilateral, minimal - hyperplasia, focal medullary, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1184	E	<b>Microscopic</b> eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic	- within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - vacuolation, periportal, mild - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1184	E	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin	- within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - fibrosis, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1184	E	<b>Microscopic</b> skin, subcutis	- lipoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- erosion/ulcer, minimal - hyperplasia, epithelial, nonglandular, moderate - inflammation, mild
		testes	- within normal limits
		thymus	- depletion, lymphoid, generalized, moderate
		thyroid gland	- hyperplasia, c-cell, focal, unilateral, minimal
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
E - Euthanized <i>in extremis</i>			



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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1184	E	<b>Microscopic</b> urinary bladder	- hyperplasia, simple transitional cell, mild - inflammation, moderate
		non-correlated macro observation	- stomach, glandular - irregular surface
		Cause of Death	- pituitary tumor
1185	D	<b>Macroscopic</b> pituitary gland	- enlarged, brown, severe
		stomach, nonglandular	- focus/foci, brown, mild
1185	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal medullary, bilateral, mild
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- compression, ventral (pituitary tumor), moderate
		coagulating glands	- within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1185	D	<b>Microscopic</b> epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - degeneration/atrophy, retina, unilateral, mild - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, periportal, mild - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1185	D	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual	- dilatation, sinus, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1185	D	<b>Microscopic</b> seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes thymus thyroid gland  tongue	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - erosion/ulcer, moderate corresponds to macroscopic observation (stomach, nonglandular - focus/foci, brown) - within normal limits - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, bilateral, primary, incidental, not cause of death - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1185	D	<b>Microscopic</b> trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1186	S	<b>Macroscopic</b> pituitary gland	- cyst, red, mild
1186	S	<b>Microscopic</b> liver  pancreas pituitary gland  testes tongue	- hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - cyst) - within normal limits - within normal limits
S - Scheduled necropsy D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1187	D	<b>Macroscopic</b> kidneys	- cyst, clear, right, mild - enlarged, bilateral, moderate
		liver	- enlarged, multiple lobes, mild
		pituitary gland	- enlarged, mild
		urinary bladder	- distended with urine, moderate
1187	D	<b>Microscopic</b> adrenal glands	- adenoma, cortical, benign, unilateral, primary, incidental, not cause of death - hyperplasia, focal medullary, unilateral, mild - hypertrophy, focal cortical, unilateral, minimal - vacuolation, focal, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits

D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1187	D	<b>Microscopic</b> epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - cyst, unilateral, mild corresponds to macroscopic observation (kidneys - cyst) - hydronephrosis, bilateral, mild corresponds to macroscopic observation (kidneys - enlarged) - nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1187	D	<b>Microscopic</b> larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular	 - within normal limits - degeneration, cystic, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits
D - Died on Study			



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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1187	D	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - polyarteritis, bilateral, mild - depletion, lymphoid, generalized, moderate - adenoma, follicular cell, benign, unilateral, primary, incidental, not cause of death - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1187	D	<b>Microscopic</b> trachea ureters urinary bladder	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- dilatation, bilateral, mild</li> <li>- dilatation, moderate corresponds to macroscopic observation (urinary bladder - distended with urine)</li> <li>- hyperplasia, simple transitional cell, minimal</li> </ul>
1188	E	non-correlated macro observation Cause of Death <b>Macroscopic</b> liver lymph node, popliteal  skin, subcutis  spleen	<ul style="list-style-type: none"> <li>- liver - enlarged</li> <li>- urogenital inflammation/obstruction/calculi</li> <li>- enlarged, multiple lobes, mild</li> <li>- within normal limits draining node for mass a, bilateral.</li> <li>- mass, tan, mass a, dorsal sacral region, present corresponds to antemortem observation (mass 1) approximately 15.0 cm in diameter.</li> <li>- enlarged, moderate</li> </ul>

E - Euthanized *in extremis*  
D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1188	E	<b>Microscopic</b> adrenal glands	- hematopoiesis, extramedullary, bilateral, mild - hyperplasia, focal medullary, bilateral, mild - vacuolation, focal, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- hyperplasia, granulocytic, mild
		bone marrow, sternum	- hyperplasia, granulocytic, mild
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, minimal
		joint, tibiofemoral	- within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1188	E	<b>Microscopic</b> kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric lymph node, popliteal nerve, sciatic nose, level a nose, level b nose, level c nose, level d	 - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1188	E	<b>Microscopic</b> pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death - atrophy, acinar, mild - fibrosis, mild
		parathyroid glands	- not examined
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		skin, subcutis	- fibrosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits

E - Euthanized *in extremis*

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1188	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen  stomach, glandular stomach, nonglandular testes thymus thyroid gland  tongue trachea ureters urinary bladder non-correlated macro observation Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, moderate corresponds to macroscopic observation (spleen - enlarged) - within normal limits - within normal limits - hyperplasia, interstitial cell, bilateral, minimal - depletion, lymphoid, generalized, moderate - adenoma, c-cell, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - liver - enlarged - fibrosarcoma/fibroma

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1189	D	<b>Macroscopic</b> all tissues	- within normal limits
1189	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1189	D	<b>Microscopic</b> heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands	- cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1189	D	<b>Microscopic</b> pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular	- within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - inflammation, subacute/chronic, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1189	D	<b>Microscopic</b> testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1190	E	<b>Macroscopic</b> liver urinary bladder	- discoloration, tan, multiple lobes, moderate - distended with urine, red, severe fur around penis stained red.
1190	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1190	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, tubular, bilateral, mild - hydronephrosis, bilateral, minimal - mineralization, tubular, bilateral, mild - within normal limits - within normal limits

E - Euthanized *in extremis*

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Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1190	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erythrocytosis/erythrophagocytosis, sinus, mild - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1190	E	<b>Microscopic</b> salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1190	E	<b>Microscopic</b> ureters  urinary bladder  non-correlated macro observation Cause of Death	- dilatation, unilateral, mild - hemorrhage, bilateral, mild hemorrhage seen with kidneys on slide 1. - hemorrhage, severe corresponds to macroscopic observation (urinary bladder - distended with urine) - inflammation, acute, mild - liver - discoloration, tan - urogenital inflammation/obstruction/calculi
1191	E	<b>Macroscopic</b> lung with bronchi urinary bladder	- focus/foci, red, multiple lobes, mild - distended with urine, red, moderate
1191	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur	- vacuolation, focal, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**

Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1191	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - hydronephrosis, bilateral, mild - nephropathy, chronic progressive, unilateral, minimal  - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1191	E	<b>Microscopic</b> large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas	- within normal limits - within normal limits - vacuolation, focal, minimal - crystals, hemoglobin, mild corresponds to macroscopic observation (lung with bronchi - focus/foci, red) - hemorrhage, mild corresponds to macroscopic observation (lung with bronchi - focus/foci, red) - histiocytosis, alveolar, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, mild

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1191	E	<b>Microscopic</b> parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	 - within normal limits one of pair present - within normal limits - hyperplasia, focal, pars distalis, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1191	E	<b>Microscopic</b> stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder	- within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, moderate corresponds to macroscopic observation (urinary bladder - distended with urine) - hemorrhage, mild corresponds to macroscopic observation (urinary bladder - distended with urine) - inflammation, minimal - urogenital inflammation/obstruction/calculi
1192	S	<b>Macroscopic</b> kidneys	- dilatation, pelvic, left, mild
1192	S	<b>Microscopic</b> kidneys	- nephropathy, chronic progressive, bilateral, mild

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1192	S	<b>Microscopic</b> liver  pancreas testes tongue non-correlated macro observation	- focus of cellular alteration, eosinophilic, minimal - hematopoiesis, extramedullary, minimal - vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - kidneys - dilatation, pelvic
1193	S	<b>Macroscopic</b> lymph node, axillary  lymph node, mesenteric  pancreas  skin	- within normal limits draining node for mass a, right. - within normal limits draining node for mass b. - mass, tan, mass b, present approximately 1.0 cm in diameter. - nodule, tan, right lateral thorax, present corresponds to antemortem observation (nodule) approximately 0.3 cm in diameter.
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1193	S	<b>Macroscopic</b> skin, subcutis	- mass, tan, mass a, right axillary area, present corresponds to antemortem observation (mass 1) approximately 3.5 cm in diameter.
1193	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - focus of cellular alteration, basophilic, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - vacuolation, focal, minimal
		lymph node, axillary	- within normal limits
		lymph node, mesenteric	- within normal limits
		pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pancreas - mass b)
		skin	- hyperplasia, acinar cell, focal, mild - keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin - nodule)
		skin, subcutis	- fibroma, benign, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a)
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1193	S	<b>Microscopic</b> testes tongue	- polyarteritis, bilateral, mild - within normal limits
1194	S	<b>Macroscopic</b> animal/whole body  lymph node, iliac  pituitary gland prostate gland	- body fat depleted, moderate corresponds to antemortem observation (thin) - within normal limits draining node for mass a, bilateral. - small, moderate - mass, tan, mass a, present approximately 3.0 x 1.5 x 1.5 cm.
1194	S	urinary bladder <b>Microscopic</b> liver  lymph node, iliac	- irregular surface, mild  - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, mild - dilatation, sinus, minimal - hyperplasia, lymphocyte/plasmacyte, medulla, mild
S - Scheduled necropsy			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1194	S	<b>Microscopic</b> pancreas pituitary gland  prostate gland  testes tongue urinary bladder	- within normal limits - fibrosis, moderate corresponds to macroscopic observation (pituitary gland - small) - macrophages, pigmented, mild - abscess, severe corresponds to macroscopic observation (prostate gland - mass a) - within normal limits - within normal limits - hyperplasia, simple transitional cell, mild - inflammation, mild - inflammation, peritoneal, mild corresponds to macroscopic observation (urinary bladder - irregular surface)
1195	E	<b>Macroscopic</b> pituitary gland ureters urinary bladder	- enlarged, minimal - distended with urine, clear, bilateral, mild - distended with urine, red, moderate

S - Scheduled necropsy  
E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1195	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands  epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral	   - pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dilatation, bilateral, mild - inflammation, bilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1195	E	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas	- dilatation, tubular, bilateral, mild - hydronephrosis, bilateral, mild - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - histiocytosis, alveolar, minimal - erythrocytosis/erythrophagocytosis, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1195	E	<b>Microscopic</b> parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles  skeletal muscle, biceps femoris skin  small intestine, duodenum small intestine, ileum small intestine, jejunum	- within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - inflammation, acute, minimal - within normal limits - within normal limits - within normal limits - dilatation, bilateral, mild - inflammation, bilateral, minimal - within normal limits - erosion/ulcer, mild - hyperplasia, epidermal, mild - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1195	E	<b>Microscopic</b> spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters  urinary bladder	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - dilatation, seminiferous tubules, unilateral, mild - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - dilatation, bilateral, moderate corresponds to macroscopic observation (ureters - distended with urine) - hemorrhage, moderate corresponds to macroscopic observation (urinary bladder - distended with urine) - hyperplasia, simple transitional cell, moderate - inflammation, moderate corresponds to macroscopic observation (urinary bladder - distended with urine)

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1195	E	<b>Microscopic</b> Cause of Death	- urogenital inflammation/obstruction/calculi
1196	E	<b>Macroscopic</b> lacrimal glands, exorbital  skin, subcutis	- not identified, left, no grade due to lesion - abscess, left lateral neck, mild corresponds to antemortem observation (hair sparse scabbed area nodule)
1196	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands	- hyperplasia, focal cortical, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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Individual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1196	E	<b>Microscopic</b> epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital  large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular	 - within normal limits - within normal limits - inflammation, unilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - histiocytosis, alveolar, minimal - dilatation, sinus, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1196	E	<b>Microscopic</b> lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d  pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris	 - within normal limits - degeneration, axonal/myelin, minimal  - within normal limits - within normal limits - exudate, nasal passage, minimal - exudate, nasal passage, minimal - inflammation, minimal  - within normal limits - within normal limits - within normal limits - hyperplasia, focal, pars distalis, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration/necrosis, myofiber, minimal

E - Euthanized *in extremis*

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1196	E	<b>Microscopic</b> skin	- carcinoma, squamous cell, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - abscess)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
		testes	- within normal limits
		thymus	- depletion, lymphoid, generalized, severe
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits one of pair present

E - Euthanized *in extremis*

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1196	E	<b>Microscopic</b> urinary bladder Cause of Death	- within normal limits - skin tumor
1197	D	<b>Macroscopic</b> lung with bronchi tongue	- focus/foci, red, multifocal, multiple lobes, mild - absent portion/cannibalized, no grade
1197	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1197	D	<b>Microscopic</b> eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, basophilic, minimal - infiltration, mononuclear cell, minimal - hemorrhage, mild corresponds to macroscopic observation (lung with bronchi - focus/foci, red) acute hemorrhage, probably associated with the dying process.
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1197	D	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a  nose, level b  nose, level c  nose, level d  pancreas  parathyroid glands  pharynx pituitary gland prostate gland salivary gland, mandibular	- within normal limits - within normal limits - within normal limits - foreign material, minimal plant material. - foreign material, moderate plant material. - foreign material, mild plant material. - foreign material, minimal plant material. - fibrosis, minimal - hyperplasia, acinar cell, focal, mild - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1197	D	<b>Microscopic</b> salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1197	D	<b>Microscopic</b> ureters urinary bladder Cause of Death	- within normal limits - within normal limits - undetermined
1198	E	<b>Macroscopic</b> foot/feet  liver stomach, nonglandular	- swollen/thickened, right, mild corresponds to antemortem observation (swelling) - discoloration, tan, multiple lobes, moderate - focus/foci, tan, mild
1198	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum bone, femur	- hyperplasia, focal medullary, unilateral, mild - pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1198	E	<b>Microscopic</b> bone, sternum brain coagulating glands epididymides  esophagus eyes eyes, optic nerves eyes, retina foot/feet galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	- within normal limits - within normal limits - within normal limits - granuloma, spermatic, unilateral, moderate - oligospermia/germ cell debris, unilateral, severe - within normal limits - within normal limits - within normal limits - within normal limits - inflammation, unilateral, moderate - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1198	E	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland	- within normal limits - degeneration, cystic, focal, mild - hyperplasia, bile duct, minimal - vacuolation, diffuse, mild corresponds to macroscopic observation (liver - discoloration, tan) - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - hyperplasia, focal, bilateral, minimal - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1198	E	<b>Microscopic</b> prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1198	E	<b>Microscopic</b> stomach, nonglandular	- erosion/ulcer, mild corresponds to macroscopic observation (stomach, nonglandular - focus/foci, tan) - hyperplasia, epithelial, nonglandular, moderate corresponds to macroscopic observation (stomach, nonglandular - focus/foci, tan) - inflammation, mild
		testes	- degeneration/atrophy, seminiferous tubules, unilateral, severe
		thymus	- granuloma, spermatic, unilateral, moderate
		thyroid gland	- depletion, lymphoid, generalized, severe
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		Cause of Death	- foot/feet; inflammation; unilateral, moderate

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1199	S	<b>Macroscopic</b> all tissues	- within normal limits
1199	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal
		pancreas	- atrophy, acinar, minimal
		testes	- within normal limits
		tongue	- within normal limits
1200	D	<b>Macroscopic</b> lymph node, axillary	- within normal limits draining node for mass a, right.
		skin	- mass, tan, mass a, dorsal thoracic region, present corresponds to antemortem observation (nodule) approximately 1.0 cm in diameter.
1200	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal cortical, unilateral, minimal - hyperplasia, focal medullary, unilateral, mild
S - Scheduled necropsy D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1200	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1200	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung lymph node, axillary lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands  pharynx	- within normal limits - within normal limits - within normal limits - infiltration, mononuclear cell, minimal - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - fibrosis, minimal - within normal limits one of pair present - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1200	D	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- degeneration/necrosis, myofiber, minimal
		skin	- keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin - mass a)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, minimal
		stomach, glandular	- within normal limits
		stomach, nonglandular	- within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1200	D	<b>Microscopic</b> testes thymus thyroid gland tongue trachea ureters  urinary bladder Cause of Death	- within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - undetermined
1201	D	<b>Macroscopic</b> pituitary gland	- enlarged, red, mild
1201	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum	- within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1201	D	<b>Microscopic</b> bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina  gall harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum	- within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1201	D	<b>Microscopic</b> larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland  prostate gland	- within normal limits - focus of cellular alteration, basophilic, minimal - hyperplasia, bile duct, mild - within normal limits - dilatation, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - adenoma, islet cell, benign, primary, incidental, not cause of death - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1201	D	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1201	D	<b>Microscopic</b> trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - pituitary tumor
1202	E	<b>Macroscopic</b> parathyroid glands pituitary gland testes thyroid gland	- enlarged, left, severe - enlarged, minimal - small, bilateral, mild - enlarged, left, severe
1202	E	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur	- hyperplasia, focal cortical, bilateral, mild - pheochromocytoma, benign, bilateral, primary, incidental, not cause of death - vacuolation, focal, unilateral, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*  
D - Died on Study



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1202	E	<b>Microscopic</b> bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, bilateral, mild - nephropathy, chronic progressive, bilateral, moderate  - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1202	E	<b>Microscopic</b> large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a   nose, level b	- within normal limits - within normal limits - degeneration, cystic, focal, minimal - infiltration, mononuclear cell, minimal - inflammation, subacute/chronic, minimal - dilatation, sinus, minimal - within normal limits - degeneration, axonal/myelin, minimal - exudate, nasal passage, moderate - foreign material, minimal plant. - fungus/yeast, moderate - inflammation, moderate - exudate, nasal passage, mild - fungus/yeast, severe - inflammation, mild
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1202	E	<b>Microscopic</b> nose, level c	- exudate, nasal passage, moderate - foreign material, minimal plant. - fungus/yeast, moderate - inflammation, mild - metaplasia, squamous, mild
		nose, level d	- exudate, nasal passage, mild - foreign material, mild plant. - inflammation, minimal
		pancreas	- hyperplasia, acinar cell, focal, mild
		parathyroid glands	- within normal limits one of pair present
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1202	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - polyarteritis, bilateral, mild - depletion, lymphoid, generalized, moderate

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1202	E	<b>Microscopic</b> thyroid gland	<ul style="list-style-type: none"> <li>- adenoma, follicular cell, benign, unilateral, primary, incidental, not cause of death</li> <li>- carcinoma, c-cell, malignant, unilateral, primary, incidental, not cause of death</li> <li>- corresponds to macroscopic observation (parathyroid glands - enlarged; thyroid gland - enlarged)</li> </ul>
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- within normal limits
		non-correlated macro observation	- testes - small
		Cause of Death	- nose/oral inflammation/ulceration
1203	D	<b>Macroscopic</b> eyes	- absent/cannibalized, left, no grade
		eyes, optic nerves	- absent/cannibalized, left, no grade
		eyes, retina	- absent/cannibalized, left, no grade
		harderian glands	- absent/cannibalized, left, no grade

E - Euthanized *in extremis*  
D - Died on Study

**Individual Animal Listing - MALE**  
Terminal

D - Died on Study

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1203	D	<b>Microscopic</b> galt harderian glands  heart joint, tibiofemoral kidneys lacrimal glands, exorbital  large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic	- within normal limits - within normal limits one of pair present - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - bacterial colonies, mild there is lysis of red blood cells in focally extensive areas indicative of dosing injury. - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1203	D	<b>Microscopic</b> nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			



MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1203	D	<b>Microscopic</b> spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1204	S	<b>Macroscopic</b> liver	- mass, tan, mass b, median lobe, present approximately 2.0 x 3.0 x 2.0 cm.
S - Scheduled necropsy D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1204	S	<b>Macroscopic</b> lymph node, hepatic	- not identified, no grade draining node for mass b.
		lymph node, inguinal	- not identified, bilateral, no grade draining node for mass a.
		skin	- mass, tan, mass a, dorsal lumbar region, present corresponds to antemortem observation (nodule) approximately 1.0 cm in diameter.
1204	S	<b>Microscopic</b> liver	- adenoma, hepatocellular, benign, primary, incidental, not cause of death corresponds to macroscopic observation (liver - mass b)
			- focus of cellular alteration, basophilic, minimal
			- focus of cellular alteration, eosinophilic, minimal
			- hyperplasia, bile duct, minimal
		pancreas	- atrophy, acinar, minimal
			- polyarteritis, minimal
		skin	- keratoacanthoma, benign, primary, mortality-independent corresponds to macroscopic observation (skin - mass a)
		testes	- polyarteritis, bilateral, minimal
S - Scheduled necropsy			

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1204	S	<b>Microscopic</b> tongue	- within normal limits
1205	D	<b>Macroscopic</b> adrenal glands lung with bronchi lymph node, mandibular  skin, subcutis   stomach, nonglandular	- enlarged, bilateral, mild - focus/foci, tan, multiple lobes, mild - enlarged, red, bilateral, mild draining node for mass a, mass b and mass c, left. draining node for mass d, right. - mass, tan, mass a, left lateral neck, present corresponds to antemortem observation (mass 1) approximately 7.0 cm in diameter. - mass, tan, mass b, left lateral neck, present approximately 2.5 x 2.0 x 2.5 cm. - mass, tan, mass c, left lateral neck, present approximately 2.7 x 1.5 x 1.0 cm. - mass, tan, mass d, right lateral neck, present approximately 1.8 x 1.2 x 1.5 cm. - irregular surface, tan, moderate

S - Scheduled necropsy  
D - Died on Study

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> adrenal glands  aorta bone marrow, femur bone marrow, sternum  bone, femur bone, sternum brain cavity, abdominal  cavity, thoracic  coagulating glands  epididymides esophagus	- hyperplasia, focal medullary, bilateral, minimal - vacuolation, diffuse, bilateral, mild - within normal limits - hyperplasia, mixed, mild - hyperplasia, mixed, mild - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, unilateral, multicentric, fatal, positive cause of death - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> eyes  eyes, optic nerves eyes, retina galt harderian glands  heart  joint, tibiofemoral kidneys  lacrimal glands, exorbital  large intestine, cecum	- sarcoma, histiocytic, malignant, unilateral, multicentric, fatal, positive cause of death periocular. - within normal limits - within normal limits - within normal limits - sarcoma, histiocytic, malignant, bilateral, multicentric, fatal, positive cause of death - cardiomyopathy, mild - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - within normal limits - hyaline, droplets, increased, bilateral, moderate - nephropathy, chronic progressive, bilateral, moderate - sarcoma, histiocytic, malignant, unilateral, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, bilateral, multicentric, fatal, positive cause of death - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> large intestine, colon large intestine, rectum  larynx liver  lung  lymph node, mandibular  lymph node, mediastinal	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death</li> <li>- within normal limits</li> <li>- degeneration, cystic, focal, minimal</li> <li>- hyperplasia, bile duct, minimal</li> <li>- vacuolation, periportal, mild</li> <li>- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death</li> <li>- corresponds to macroscopic observation (lung with bronchi - focus/foci, tan)</li> <li>- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death</li> <li>- corresponds to macroscopic observation (lymph node, mandibular - enlarged)</li> <li>- dilatation, sinus, moderate</li> <li>- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death</li> <li>- slide 14.</li> </ul>
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> lymph node, mesenteric  multicentric neoplasm  nerve, sciatic nose, level a  nose, level b  nose, level c  nose, level d  pancreas  parathyroid glands pharynx pituitary gland	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - within normal limits - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death - not examined - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> prostate gland	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		salivary gland, mandibular	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		salivary gland, parotid	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- sarcoma, histiocytic, malignant, unilateral, multicentric, fatal, positive cause of death
		skeletal muscle, biceps femoris	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		skin	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> skin, subcutis	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death corresponds to macroscopic observation (skin, subcutis - mass a; skin, subcutis - mass b; skin, subcutis - mass c; skin, subcutis - mass d)
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- hematopoiesis, extramedullary, increased, mild
		stomach, glandular	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		stomach, nonglandular	- erosion/ulcer, moderate corresponds to macroscopic observation (stomach, nonglandular - irregular surface)
		testes	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1205	D	<b>Microscopic</b> thymus	- depletion, lymphoid, generalized, severe - sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		thyroid gland	- within normal limits
		tongue	- within normal limits
		trachea	- within normal limits
		ureters	- within normal limits
		urinary bladder	- sarcoma, histiocytic, malignant, multicentric, fatal, positive cause of death
		non-correlated macro observation	- adrenal glands - enlarged
		Cause of Death	- histiocytic sarcoma
1206	E	<b>Macroscopic</b> liver	- focus/foci, tan, median lobe, mild
		pituitary gland	- enlarged, brown, severe
1206	E	<b>Microscopic</b> adrenal glands	- hyperplasia, focal cortical, unilateral, minimal

E - Euthanized *in extremis*  
D - Died on Study

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1206	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves  eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, unilateral, minimal - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1206	E	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands  pharynx	 - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - atrophy, acinar, minimal - fibrosis, minimal - within normal limits one of pair present - within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1206	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits

E - Euthanized *in extremis*

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1206	E	<b>Microscopic</b> stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder non-correlated macro observation Cause of Death	- within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - liver - focus/foci, tan - pituitary tumor
1207	D	<b>Macroscopic</b> lung with bronchi	- discoloration, red, multiple lobes, moderate
1207	D	<b>Microscopic</b> adrenal glands  aorta	- within normal limits no medulla present - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1207	D	<b>Microscopic</b> bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1207	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland prostate gland	- within normal limits - within normal limits - within normal limits - within normal limits - bacterial colonies, mild discoloration is postmortem congestion - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits one of pair present - within normal limits - within normal limits - within normal limits
D - Died on Study			



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1207	D	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1207	D	<b>Microscopic</b> trachea ureters urinary bladder non-correlated macro observation Cause of Death	- within normal limits - within normal limits - within normal limits - lung with bronchi - discoloration, red - probable dosing injury
1208	D	<b>Macroscopic</b> all tissues	- within normal limits
1208	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1208	D	<b>Microscopic</b> epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - hyperplasia, bile duct, minimal - histiocytosis, alveolar, minimal focal areas with lysis of red blood cells.
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1208	D	<b>Microscopic</b> lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - inflammation, acute, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1208	D	<b>Microscopic</b> skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - probable dosing injury
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in RatsIndividual Animal Listing - MALE  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1209	E	<b>Macroscopic</b> pituitary gland stomach, nonglandular	- enlarged, red, severe - focus/foci, red, mild
1209	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - depletion, secretory, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1209	E	<b>Microscopic</b> heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b	- cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - focus of cellular alteration, eosinophilic, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - histiocytosis, alveolar, minimal - erythrocytosis/erythrophagocytosis, sinus, mild - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1209	E	<b>Microscopic</b> nose, level c	- exudate, nasal passage, mild - foreign material, minimal plant.
		nose, level d	- exudate, nasal passage, mild - foreign material, minimal plant.
		pancreas	- adenoma, islet cell, benign, primary, incidental, not cause of death - hyperplasia, islet cell, minimal
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits

E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1209	E	<b>Microscopic</b> seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular  testes	- depletion, secretory, bilateral, moderate - degeneration/necrosis, myofiber, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - erosion/ulcer, moderate corresponds to macroscopic observation (stomach, nonglandular - focus/foci, red) - hyperplasia, epithelial, nonglandular, moderate corresponds to macroscopic observation (stomach, nonglandular - focus/foci, red) - inflammation, mild - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1209	E	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1210	E	<b>Macroscopic</b> lymph node, inguinal  pituitary gland skin, subcutis	- within normal limits draining node for mass a, left. - enlarged, red, severe - mass, ulcerated, mass a, left inguinal area, present corresponds to antemortem observation (mass 1) approximately 4.5 cm in diameter, tan.
1210	E	<b>Microscopic</b> adrenal glands	- pheochromocytoma, benign, unilateral, primary, incidental, not cause of death - vacuolation, focal, unilateral, minimal

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1210	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, mild - within normal limits - hydronephrosis, bilateral, minimal - hyperplasia, transitional cell, unilateral, minimal - nephropathy, chronic progressive, bilateral, minimal
E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1210	E	<b>Microscopic</b> lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, inguinal lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - necrosis, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - exudate, nasal passage, minimal - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1210	E	<b>Microscopic</b> pancreas parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin skin, subcutis  small intestine, duodenum small intestine, ileum	- fibrosis, minimal - within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosarcoma, malignant, primary, mortality-independent corresponds to macroscopic observation (skin, subcutis - mass a) - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1210	E	<b>Microscopic</b> small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - hyperplasia, c-cell, focal, bilateral, mild - within normal limits - within normal limits - dilatation, unilateral, mild - within normal limits - fibrosarcoma/fibroma
1211	S	<b>Macroscopic</b> small intestine, ileum	- intussusception, moderate

S - Scheduled necropsy  
E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1211	S	<b>Microscopic</b> liver  pancreas  small intestine, ileum  testes tongue	- degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - fibrosis, minimal - hyperplasia, acinar cell, focal, mild - hyperplasia, islet cell, mild - adenocarcinoma, malignant, primary, incidental, not cause of death corresponds to macroscopic observation (small intestine, ileum - intussusception) - within normal limits - within normal limits
1212	S	<b>Macroscopic</b> bile duct, extrahepatic pituitary gland	- dilatation, mild - enlarged, red, severe
S - Scheduled necropsy			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1212	S	<b>Microscopic</b> bile duct, extrahepatic	- calculus/calculi, moderate - dilatation, moderate corresponds to macroscopic observation (bile duct, extrahepatic - dilatation) - hyperplasia, mild - hematopoiesis, extramedullary, minimal - atrophy, acinar, minimal - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits
1213	E	<b>Macroscopic</b> liver pituitary gland	- focus/foci, tan, median lobe, mild - enlarged, severe
1213	E	<b>Microscopic</b> adrenal glands	- vacuolation, focal, unilateral, minimal

S - Scheduled necropsy  
E - Euthanized *in extremis*



MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1213	E	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, focal, unilateral, mild - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1213	E	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx	- within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - vacuolation, median cleft, mild corresponds to macroscopic observation (liver - focus/foci, tan) - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1213	E	<b>Microscopic</b> pituitary gland	- adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged)
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
		skeletal muscle, biceps femoris	- within normal limits
		skin	- within normal limits
		small intestine, duodenum	- within normal limits
		small intestine, ileum	- within normal limits
		small intestine, jejunum	- within normal limits
		spinal cord, cervical	- within normal limits
		spinal cord, lumbar	- within normal limits
		spinal cord, thoracic	- within normal limits
		spleen	- within normal limits
		stomach, glandular	- within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1213	E	<b>Microscopic</b> stomach, nonglandular  testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- hyperplasia, epithelial, nonglandular, moderate - inflammation, mild - dilatation, seminiferous tubules, unilateral, mild - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - pituitary tumor
1214	D	<b>Macroscopic</b> foot/feet  lymph node, mesenteric	- ulcer, plantar/palmar, minimal corresponds to antemortem observation (nodule) - enlarged, moderate
1214	D	<b>Microscopic</b> adrenal glands	- within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1214	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina  galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined autolysis too severe for diagnosis - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1214	D	<b>Microscopic</b> large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric  nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands	- within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - vacuolation, centrilobular, mild - within normal limits - within normal limits - dilatation, sinus, moderate corresponds to macroscopic observation (lymph node, mesenteric - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits one of pair present
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1214	D	<b>Microscopic</b> pharynx pituitary gland prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes	- within normal limits - hyperplasia, focal, pars distalis, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, increased, minimal - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1214	D	<b>Microscopic</b> thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
1215	D	<b>Macroscopic</b> adipose tissue  heart testes	- focus/foci, red, mild located near right testicle. - focus/foci, red, right ventricle, mild - focus/foci, red, right, mild
1215	D	<b>Microscopic</b> adipose tissue	- within normal limits red discoloration is blood within blood vessels, not a lesion.
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1215	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal cortical, bilateral, mild - vacuolation, focal, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- within normal limits
		heart	- cardiomyopathy, mild
		joint, tibiofemoral	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1215	D	<b>Microscopic</b> kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver lung lymph node, mandibular lymph node, mesenteric  nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas	- hydronephrosis, bilateral, minimal - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hemangiosarcoma, malignant, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1215	D	<b>Microscopic</b> parathyroid glands  pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen	- within normal limits one of pair present - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1215	D	<b>Microscopic</b> stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder non-correlated macro observation  Cause of Death	- within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - adipose tissue - focus/foci, red - heart - focus/foci, red - testes - focus/foci, red - undetermined
1216	D	<b>Macroscopic</b> all tissues	- within normal limits
1216	D	<b>Microscopic</b> adrenal glands	- within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1216	D	<b>Microscopic</b> aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - astrocytoma, malignant, primary, fatal, positive cause of death - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, minimal - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1216	D	<b>Microscopic</b> large intestine, colon large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland	- within normal limits - within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - necrosis, focal, minimal - vacuolation, focal, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - not examined - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1216	D	<b>Microscopic</b> prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland	 - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, moderate - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1216	D	<b>Microscopic</b> tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - brain tumor
1217	E	<b>Macroscopic</b> kidneys pituitary gland urinary bladder	- irregular surface, bilateral, mild - enlarged, red, moderate - distended with urine, moderate
1217	E	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur bone, sternum	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
E - Euthanized <i>in extremis</i> D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1217	E	<b>Microscopic</b> brain coagulating glands epididymides esophagus eyes  eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon	- compression, ventral (pituitary tumor), mild - within normal limits - within normal limits - within normal limits - cataract, bilateral, moderate - inflammation, acute, bilateral, moderate - within normal limits - fold/rosette, retinal, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - mineralization, tubular, bilateral, minimal - nephropathy, chronic progressive, bilateral, severe corresponds to macroscopic observation (kidneys - irregular surface) - within normal limits - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1217	E	<b>Microscopic</b> large intestine, rectum larynx liver  lung lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas  parathyroid glands pharynx pituitary gland  prostate gland	- within normal limits - within normal limits - hematopoiesis, extramedullary, minimal - hyperplasia, bile duct, minimal - within normal limits - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits - carcinoma, islet cell, malignant, primary, incidental, not cause of death - hyperplasia, diffuse, bilateral, minimal - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - inflammation, chronic-active, moderate

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1217	E	<b>Microscopic</b> salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue	- within normal limits - within normal limits - within normal limits - inflammation, bilateral, minimal - within normal limits - erosion/ulcer, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - gastropathy, uremic, minimal - within normal limits - hyperplasia, interstitial cell, unilateral, minimal - depletion, lymphoid, generalized, severe - within normal limits - within normal limits

E - Euthanized *in extremis*

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1217	E	<b>Microscopic</b> trachea ureters urinary bladder	<ul style="list-style-type: none"> <li>- within normal limits</li> <li>- within normal limits</li> <li>- dilatation, moderate corresponds to macroscopic observation (urinary bladder - distended with urine)</li> <li>- hyperplasia, simple transitional cell, moderate</li> <li>- inflammation, mild</li> <li>- chronic progressive nephropathy/uremia</li> </ul>
1218	S	<b>Macroscopic</b> all tissues	<ul style="list-style-type: none"> <li>- within normal limits</li> </ul>
1218	S	<b>Microscopic</b> liver  pancreas testes	<ul style="list-style-type: none"> <li>- hematopoiesis, extramedullary, minimal</li> <li>- hyperplasia, bile duct, minimal</li> <li>- vacuolation, periportal, minimal</li> <li>- atrophy, acinar, severe</li> <li>- polyarteritis, bilateral, minimal</li> </ul>
S - Scheduled necropsy E - Euthanized <i>in extremis</i>			

MPI Research Study Number 125-141  
Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1218	S	<b>Microscopic</b> tongue	- within normal limits
1219	D	<b>Macroscopic</b> lymph node, mandibular	- discoloration, red, bilateral, mild
1219	D	<b>Microscopic</b> adrenal glands	- angiectasis/cystic degeneration, focal cortical, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
S - Scheduled necropsy D - Died on Study			

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1219	D	<b>Microscopic</b> eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimial glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung	- within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - mineralization, pelvic, unilateral, minimal - nephropathy, chronic progressive, bilateral, mild - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - hyperplasia, bile duct, minimal - infiltration, mononuclear cell, minimal - vacuolation, median cleft, mild - vacuolation, periportal, mild - hypertrophy/hyperplasia, bronchiolar/bronchial, mild - inflammation, subacute/chronic, minimal
D - Died on Study			

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Dupont-18405-1238  
H-28548: Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1219	D	<b>Microscopic</b> lymph node, mandibular	- erythrocytosis/erythrophagocytosis, sinus, mild corresponds to macroscopic observation (lymph node, mandibular - discoloration, red)
		lymph node, mesenteric	- within normal limits
		nerve, sciatic	- within normal limits
		nose, level a	- within normal limits
		nose, level b	- within normal limits
		nose, level c	- within normal limits
		nose, level d	- within normal limits
		pancreas	- within normal limits
		parathyroid glands	- within normal limits
		pharynx	- within normal limits
		pituitary gland	- adenoma, pars distalis, benign, primary, incidental, not cause of death
		prostate gland	- within normal limits
		salivary gland, mandibular	- within normal limits
		salivary gland, parotid	- within normal limits
		salivary gland, sublingual	- within normal limits
		seminal vesicles	- within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1219	D	<b>Microscopic</b> skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - undetermined
D - Died on Study			



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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1220	D	<b>Macroscopic</b> pituitary gland	- enlarged, red, moderate
1220	D	<b>Microscopic</b> adrenal glands	- hyperplasia, focal cortical, unilateral, minimal - vacuolation, focal, unilateral, minimal
		aorta	- within normal limits
		bone marrow, femur	- within normal limits
		bone marrow, sternum	- within normal limits
		bone, femur	- within normal limits
		bone, sternum	- within normal limits
		brain	- within normal limits
		coagulating glands	- within normal limits
		epididymides	- within normal limits
		esophagus	- within normal limits
		eyes	- within normal limits
		eyes, optic nerves	- within normal limits
		eyes, retina	- within normal limits
		galt	- within normal limits
		harderian glands	- hyperplasia, focal, unilateral, minimal
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1220	D	<b>Microscopic</b> heart joint, tibiofemoral kidneys lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx liver  lung  lymph node, mandibular lymph node, mesenteric nerve, sciatic nose, level a nose, level b nose, level c nose, level d	- cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - degeneration, cystic, focal, minimal - focus of cellular alteration, eosinophilic, minimal - inflammation, perivascular, mild - macrophages, alveolar, mild - within normal limits - within normal limits - degeneration, axonal/myelin, minimal - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1220	D	<b>Microscopic</b> pancreas parathyroid glands pharynx pituitary gland  prostate gland salivary gland, mandibular salivary gland, parotid salivary gland, sublingual seminal vesicles skeletal muscle, biceps femoris skin small intestine, duodenum small intestine, ileum small intestine, jejunum spinal cord, cervical spinal cord, lumbar	- atrophy, acinar, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1220	D	<b>Microscopic</b> spinal cord, thoracic spleen stomach, glandular stomach, nonglandular testes thymus thyroid gland tongue trachea ureters urinary bladder Cause of Death	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - depletion, lymphoid, generalized, severe - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - dosing injury
1221	S	<b>Macroscopic</b> pituitary gland	- enlarged, red, moderate
1221	S	<b>Microscopic</b> liver	- degeneration, cystic, focal, minimal - hematopoiesis, extramedullary, minimal - vacuolation, periportal, minimal
S - Scheduled necropsy D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u>			
1221	S	<b>Microscopic</b> pancreas pituitary gland  testes tongue	- within normal limits - adenoma, pars distalis, benign, primary, incidental, not cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits - within normal limits
1222	D	<b>Macroscopic</b> mammary gland pituitary gland	- swollen/thickened, tan, generalized, mild - enlarged, tan, moderate
1222	D	<b>Microscopic</b> adrenal glands aorta bone marrow, femur bone marrow, sternum bone, femur	- within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
S - Scheduled necropsy D - Died on Study			

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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1222	D	<b>Microscopic</b> bone, sternum brain coagulating glands epididymides esophagus eyes eyes, optic nerves eyes, retina galt harderian glands heart joint, tibiofemoral kidneys  lacrimal glands, exorbital large intestine, cecum large intestine, colon large intestine, rectum larynx	- within normal limits - compression, ventral (pituitary tumor), moderate - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - cardiomyopathy, minimal - within normal limits - nephropathy, chronic progressive, bilateral, mild - pyelitis, unilateral, minimal - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits
D - Died on Study			

MPI Research Study Number 125-141  
Dupont-18405-1238  
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**Individual Animal Listing - MALE**  
Terminal

Group, Animal Number	Fate	Tissue	Observations
<u>1 mg/kg/day</u> 1222	D	<b>Microscopic</b> liver lung lymph node, mandibular lymph node, mesenteric mammary gland  nerve, sciatic nose, level a nose, level b nose, level c nose, level d pancreas parathyroid glands pharynx pituitary gland  prostate gland	- vacuolation, periportal, minimal - within normal limits - within normal limits - within normal limits - dilatation, gland/lumen, mild corresponds to macroscopic observation (mammary gland - swollen/thickened) - within normal limits - within normal limits - within normal limits - within normal limits - within normal limits - fibrosis, minimal - within normal limits - within normal limits - adenoma, pars distalis, benign, primary, fatal, positive cause of death corresponds to macroscopic observation (pituitary gland - enlarged) - within normal limits
D - Died on Study			